THE HELICOBACTER ERADICATION ASPIRIN TRIAL (HEAT):

DEMOGRAPHIC DATA FOR RANDOMISED (*H. pylori* POSITIVE) PATIENTS

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1. Introduction

The Helicobacter Eradication Aspirin Trial (HEAT) is a multicentre, double blind, randomised controlled trial investigating whether *Helicobacter pylori* eradication reduces the incidence of hospitalisation for peptic ulcer bleeding [1].

2. Background

- HEAT is being conducted in GP practices across the whole of the UK
- HEAT is important medically because aspirin is so widely used, and methodologically as, if successful, it will demonstrate that large-scale studies of important clinical outcomes can be conducted at a fraction of the cost of those conducted by industry
- The primary endpoint of the study is the rate of hospitalisation due to definite or probable peptic ulcer bleeding
- The study will end when 87 adjudicated events have occurred

3. Methods

- Participants are aged over 60, taking low dose aspirin for at least four months at the time of recruitment; all participants were recruited from primary care.
- Participants testing positive for *H. pylori* were randomised to receive one week active trial treatment (lansoprazole 30mg, clarithromycin 500mg and metronidazole 400mg twice daily) or placebo
- Participants are followed up using a bespoke web-based trial management system that communicates directly with HEAT Toolkit software downloaded at contributing GP practices, which issues electronic queries searching follow-up criteria
- Events are tracked by accumulating information from electronic searches of GP databases via the HEAT toolkit, patient contact, review of national Hospital Episode Statistics secondary care admission and ONS mortality data

4. Results

- Recruitment to the trial started in 2012 and completed in 2017; follow-up is endpoint driven and is ongoing
- HEAT is the largest CRN CTIMP trial, with 188,428 invitation letters sent from 1,208 practices
- A total of 37,247 positive responses were received, representing a 20% response rate
- 30,025 participants were consented to the study of whom 5,356 *H. pylori* positive participants were randomised.
- The mean age at randomisation for the *H pylori*-positive participants was 73.6 ± 7.0 (SD) years, and 73.8% of participants were male. Only 7.2% of participants were smokers although 52.9% were ex-smokers
- Recruitment figures for English participants were analysed with respect to Multiple Deprivation Indices (MDI) [4] of the GP practices. MDI=1 represents the 10% most deprived and MDI=10 is the 10% least deprived

5. Conclusion

The trial methodology has shown that recruitment of large numbers of participants from primary care is attainable, with the assistance of the NIHR Clinical Research Network, and could be applied to other outcomes studies at relatively low cost.
Last year, there were almost 17,000 hospital admissions for gastric ulcers [2] and more than 1,850 recorded deaths [3] for gastric and duodenal ulcers. If successful, the study will help to reduce NHS costs and improve health outcomes by reducing hospital admissions, increasing patient safety and preventing premature deaths.

Fig 1a

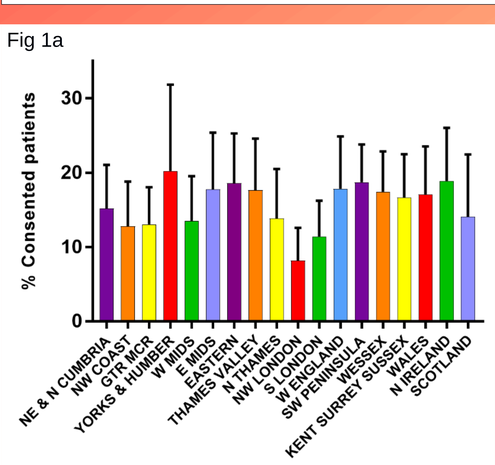

Fig 1b

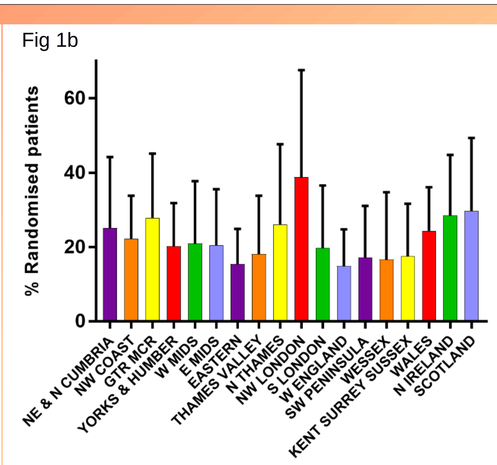

Figure 1: Participant recruitment by CRN region
Figures show the mean ± SD of percentages calculated for each contributing GP practice in the respective CRN regions

Fig 1a shows HEAT participants consented in each CRN region expressed as a percentage of the number of invitation letters sent out by each contributing practice in each region

Fig 1b shows randomised participants (ie *H pylori* positive) in each CRN region expressed as a percentage of the number of consented participants. The percent of *H. pylori* positive participants varied from 13% to 39% throughout the country

The NIHR CRN in England and the Health Boards in Wales, Scotland and Northern Ireland have played a large role in facilitating the trial and have enabled us to recruit all over the UK

Fig 2a

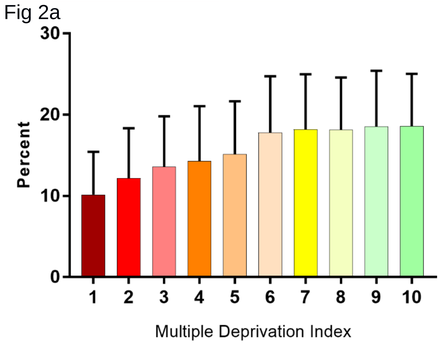

Fig 2b

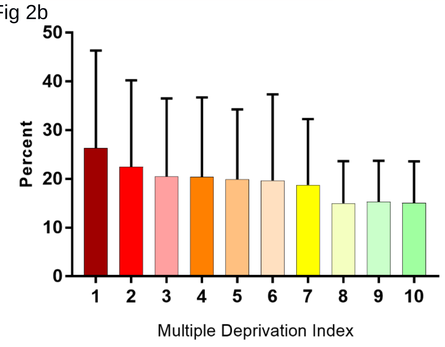

Figure 2: Participant recruitment in England with respect to the Multiple Deprivation Index of their respective GP practices
Figures show the mean ± SD of percentages calculated for each contributing GP practice in the respective MDI category

Fig 2a shows participants attending HEAT consent clinics expressed as a percentage of the number of invitation letters sent

Fig 2b shows HEAT randomised participants expressed as a percentage of the number of participants attending consent clinics

The percentage of participants attending consent visits with respect to the number of invitation letters sent out by the practices increased with a lesser amount of deprivation (Fig 2a), but the percentage of randomised participants decreased (Fig 2b)

Ref: 1. Dumbleton JS, Avery AJ, Coupland C, Hobbs FDR, Kendrick D, Moore MV, et al. 2015. The Helicobacter Eradication Aspirin Trial (HEAT): A large simple randomised controlled trial using novel methodology in primary care. EBioMedicine 2, 1200-1204.
2. NHS Digital, Hospital Admitted Patient Care Activity, 2016-17
3. Office for National Statistics, Death Registrations Summary Statistics, England and Wales, 2016
4. The English Index of Multiple Deprivation (IMD) 2015 – Guidance. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/464430/English_Index_of_Multiple_Deprivation_2015_-_Guidance.pdf

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